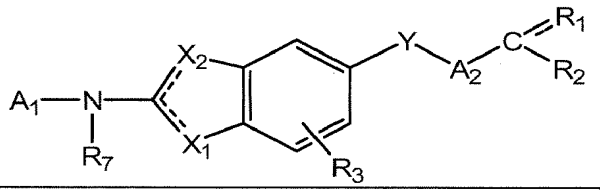
AMENDMENTS TO THE CLAIMS

1. - 73. (Cancelled)

74. (Currently amended) A method of ~~inhibiting~~ treating a disease modulated by Raf kinase activity in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound of ~~claims 1, 16, 30, 44 or 58 effective to inhibit Raf kinase activity in the human or animal subject~~ the formula (I) effective to inhibit Raf kinase activity in a human or animal subject:



(I)

wherein, X_1 and X_2 are =N- or -NR_4-, provided that if X_1 is -NR_4-, then X_2 is =N-, or if X_2 is -NR_4-, then X_2 is =N-;

Y is O or S;

A_1 is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A_2 is substituted or unsubstituted heteroaryl;

R_1 is O or H, and R_2 is NR_5 R_6 or hydroxyl; or R_1 is taken together with R_2 to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R_3 is hydrogen, halogen, loweralkyl, or loweralkoxy;

R_4 is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl;

R_5 and R_6 are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl,

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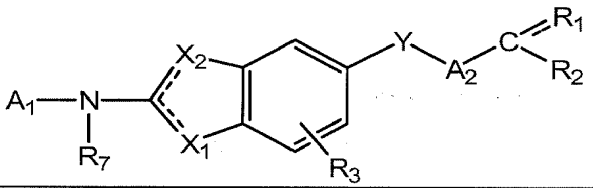
alkyloxyalkylheterocyclo, and heteroarylalkyl; or R_5 and R_6 are taken together to form substituted or unsubstituted heterocyclo or heteroaryl; and

R_7 is loweralkyl;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

75. (Currently amended) A method for treating a Ras/mitogen-activated protein kinase signal pathway-mediated cancer disorder in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound of ~~claims 1, 16, 30, 44 or 58 effective to inhibit Raf kinase activity in the human or animal subject~~ the formula (I) effective to inhibit Raf kinase activity in a human or animal subject:



(I)

wherein, X_1 and X_2 are =N- or -NR_4-, provided that if X_1 is -NR_4-, then X_2 is =N-, or if X_2 is -NR_4-, then X_2 is =N-;

Y is O or S;

A_1 is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A_2 is substituted or unsubstituted heteroaryl;

R_1 is O or H, and R_2 is NR_5 R_6 or hydroxyl; or R_1 is taken together with R_2 to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R_3 is hydrogen, halogen, loweralkyl, or loweralkoxy;

R_4 is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl;

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R_5 and R_6 are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R_5 and R_6 are taken together to form substituted or unsubstituted heterocyclo or heteroaryl; and

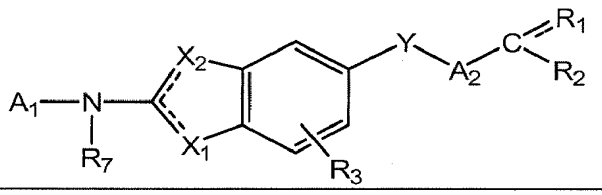
R_7 is loweralkyl;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

76. (Original) A method of claim 75 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer.

77. (Original) A method of claim 76 in which the at least one additional agent for the treatment of cancer is selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

78. (Currently amended) A method for treating a Ras/mitogen-activated protein kinase signal pathway-mediated hormone dependent cancer disorder in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound of ~~claims 1, 16, 30, 44 or 58 effective to inhibit Raf kinase activity in the human or animal subject~~ the formula (I) effective to inhibit Raf kinase activity in a human or animal subject:



(I)

wherein, X_1 and X_2 are =N- or -NR_4-, provided that if X_1 is -NR_4-, then X_2 is =N-, or if X_2 is -NR_4-, then X_2 is =N-;

Y is O or S;

A_1 is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl,

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cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A_2 is substituted or unsubstituted heteroaryl;

R_1 is O or H, and R_2 is NR_5 R_6 or hydroxyl; or R_1 is taken together with R_2 to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R_3 is hydrogen, halogen, loweralkyl, or loweralkoxy;

R_4 is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl;

R_5 and R_6 are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R_5 and R_6 are taken together to form substituted or unsubstituted heterocyclo or heteroaryl; and

R_7 is loweralkyl;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

79. (Original) A method of claim 78 wherein the hormone dependent cancer is breast cancer or prostate cancer.

80. (Original) A method of claim 78 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer.

81. (Original) A method of claim 80 in which the at least one additional agent for the treatment of cancer is selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

82. (Currently amended) A method for treating a Ras/mitogen-activated protein kinase signal pathway-mediated hematological cancer disorder in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound of ~~claims 1, 16, 30, 44 or 58 effective to inhibit Raf kinase activity in the human or animal subject~~ the formula (I) effective to inhibit Raf kinase activity in a human or animal subject:

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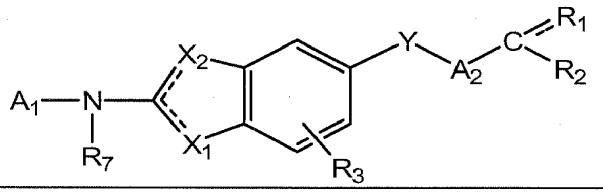

(I)

wherein, X_1 and X_2 are =N- or -NR_4-, provided that if X_1 is -NR_4-, then X_2 is =N-, or if X_2 is -NR_4-, then X_2 is =N-;

Y is O or S;

A_1 is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A_2 is substituted or unsubstituted heteroaryl;

R_1 is O or H, and R_2 is NR_5 R_6 or hydroxyl; or R_1 is taken together with R_2 to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R_3 is hydrogen, halogen, loweralkyl, or loweralkoxy;

R_4 is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl;

R_5 and R_6 are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R_5 and R_6 are taken together to form substituted or unsubstituted heterocyclo or heteroaryl; and

R_7 is loweralkyl;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

83. (Original) A method of claim 82 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer.

84. (Original) A method of claim 83 in which the at least one additional agent for the treatment of cancer is selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil,

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leucovorin carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

85-86. (Canceled)

87. (New) A method of claims 74 through 84, wherein X_1 is NR_4 and X_2 is N in formula (I).

88. (New) A method of claims 74 through 84, wherein R_4 in formula (I) is hydrogen or C_{1-6} alkyl.

89. (New) A method of claim 88, wherein R_4 in formula (I) is methyl.

90. (New) A method of claims 74 through 84, wherein Y in formula (I) is O.

91. (New) A method of claims 74 through 84, wherein A_1 in formula (I) is substituted or unsubstituted C_{3-14} aryl.

92. (New) A method of claim 91, wherein A_1 in formula (I) is selected from the group consisting of substituted or unsubstituted phenyl, pyridyl, pyrimidinyl, phenylalkyl, pyridylalkyl, pyrimidinylalkyl, heterocyclylcarbonylphenyl, heterocyclylphenyl, heterocyclylalkylphenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkylbenzoate, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, thiophene, thiophene-2-carboxylate, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, indenyl, 2,3-dihydroindenyl, tetralinyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, morpholinyl, N-piperazinyl, N-morpholinylalkyl, piperazinylalkyl, cyclohexylalkyl, indolyl, 2,3-dihydroindolyl, 1-aceyt1-2,3-dihydroindolyl, cycloheptyl, bicyclo[2.2.1]hept-2-yl, hydroxyphenyl, hydroxyalkylphenyl, pyrrolidinyl, pyrrolidin-1-yl, pyrrolidin-1-ylalkyl, 4-amino(imino)methylphenyl, isoxazolyl, indazolyl, adamantyl, bicyclohexyl, quinuclidinyl,

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imidazolyl, benzimidazolyl, imidazolylphenyl, phenylimidazolyl, pthalamido, napthyl, benzophenone, anilinyl, anisolyl, quinolinyl, quinolinonyl, phenylsulfonyl, phenylalkylsulfonyl, 9H-flouren-1-yl, piperidin-1-yl, piperidin-1-ylalkyl, cyclopropyl, cyclopropylalkyl, pyrimidin-5-ylphenyl, quinolidinylphenyl, furanyl, furanylphenyl, N-methylpiperidin-4-yl, pyrrolidin-4-ylpyridinyl, 4-diazepan-1-yl, hydroxypyrrolidn-1-yl, dialkylaminopyrrolidin-1-yl, 1,4'-bipiperidin-1'-yl, and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

93. (New) A method of claims 74 through 84, wherein A_1 in formula (I) is selected from the group consisting of substituted or unsubstituted phenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, hydroxyphenyl, hydroxyalkylphenyl, 4-amino(imino)methylphenyl and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

94. (New) A method of claim 93, wherein A_1 in formula (I) is 4-bromophenyl.

95. (New) A method of claim 93, wherein A_1 in formula (I) is trifluoromethylchlorophenyl.

96. (New) A method of claims 74 through 84, wherein A_2 in formula (I) is selected from the group consisting of substituted or unsubstituted phenyl, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinolinyl, purinyl, naphthyl, benzothiazolyl, benzopyridyl and benzoimidazolyl.

97. (New) A method of claim 95, wherein A_2 in formula (I) is pyridyl.

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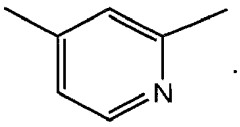
98. (New) A method of claim 96, wherein A_2 in formula (I) is 

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99. (New) A method of claims 74 through 84, wherein R_1 is taken together with R_2 in formula (I) to form a substituted or unsubstituted C_{3-8} heterocycloalkyl or C_{3-14} heteroaryl group.

100. (New) A method of claims 74 through 84, wherein R_1 is taken together with R_2 in formula (I) to form a group selected from substituted or unsubstituted phenyl, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinolinyl, purinyl, naphthyl, benzothiazolyl, benzopyridyl and benzoimidazolyl.

101. (New) A method of claims 74 through 84, wherein R_1 is taken together with R_2 in formula (I) to form a substituted or unsubstituted imidazolyl group.

102. (New) A method of claim 100, wherein the imidazolyl group is substituted with a halo C_{1-6} alkyl group.

103. (New) A method of claim 100, wherein the imidazolyl group is substituted with a trifluoromethyl group.

104. (New) A method of claims 74 through 84, wherein R_3 in formula (I) is hydrogen.

105. (New) A method of claims 74 through 84, wherein R_4 in formula (I) is hydrogen.

106. (New) A method of claims 74 through 84, wherein R_5 and R_6 in formula (I) are independently selected from hydrogen and methyl.

107. (New) A method of claim 75 wherein the Ras/mitogen-activated protein kinase signal pathway-mediated cancer disorder is selected from the group consisting of melanoma, lung cancer, pancreatic cancer, thyroid cancer, bladder cancer, colon cancer, liver cancer, myeloid leukemia and villous colon adenoma.

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